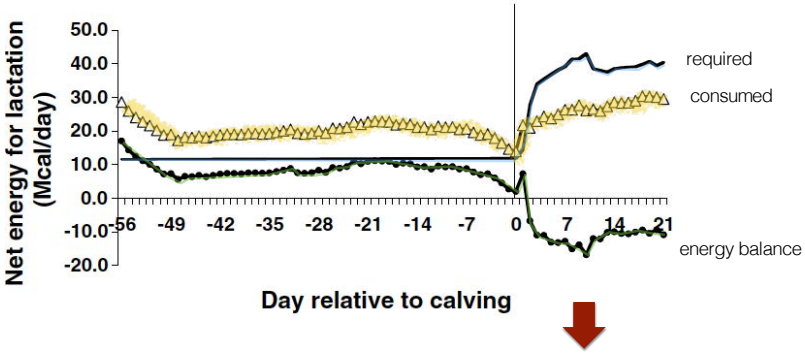
The Dual Essentiality of Choline and Methionine

Dr. Heather White
Associate Professor, Department of Dairy Science
Dairy Innovation Hub Faculty Director
University of Wisconsin-Madison

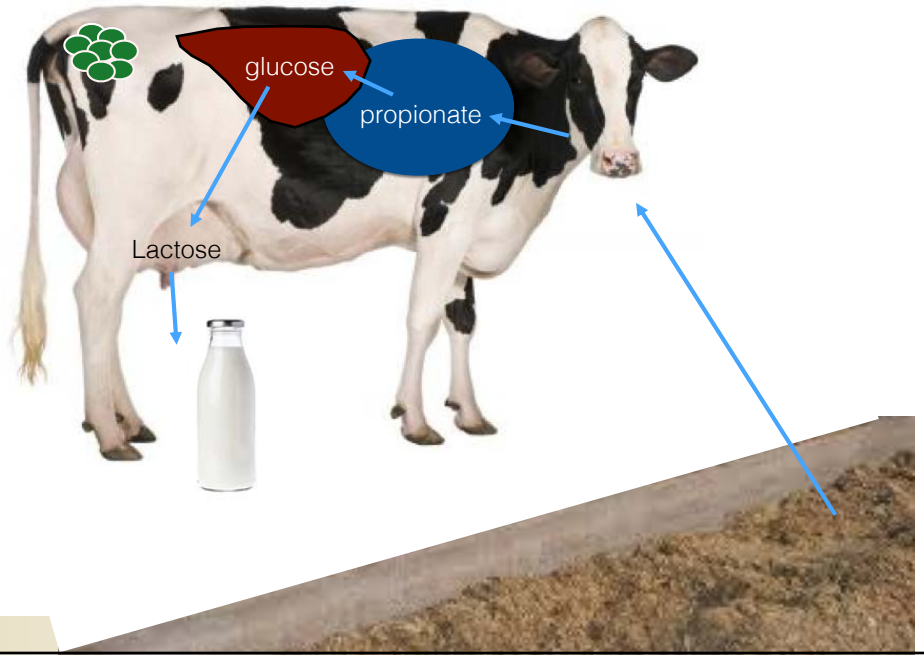
Transition to Lactation Period



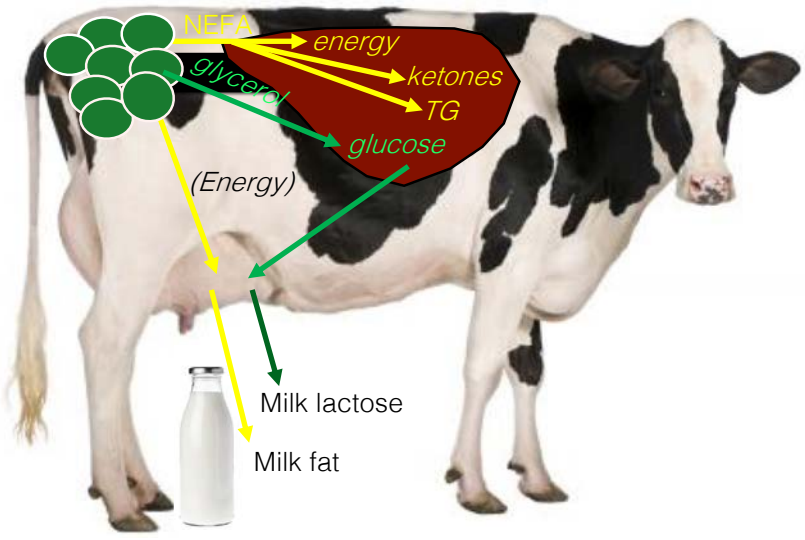
Negative Energy Balance
Negative Macronutrient balance
Negative Micronutrient balance

Grummer, 2008.

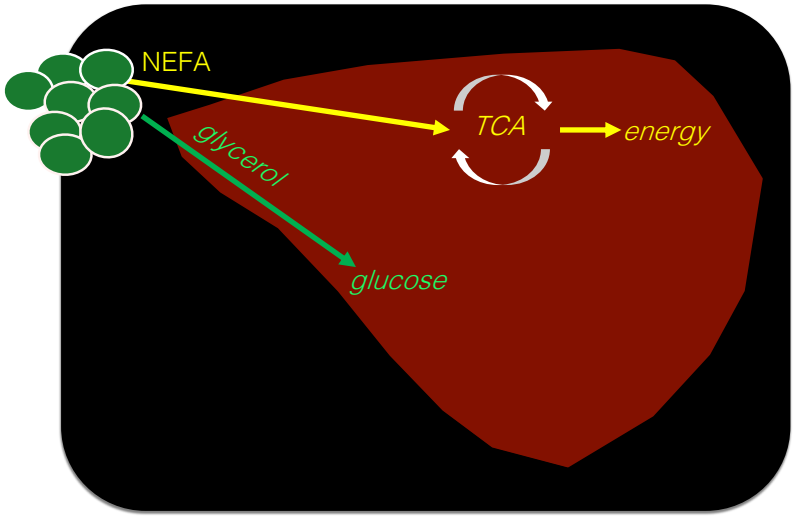
Glucose Production from Feed



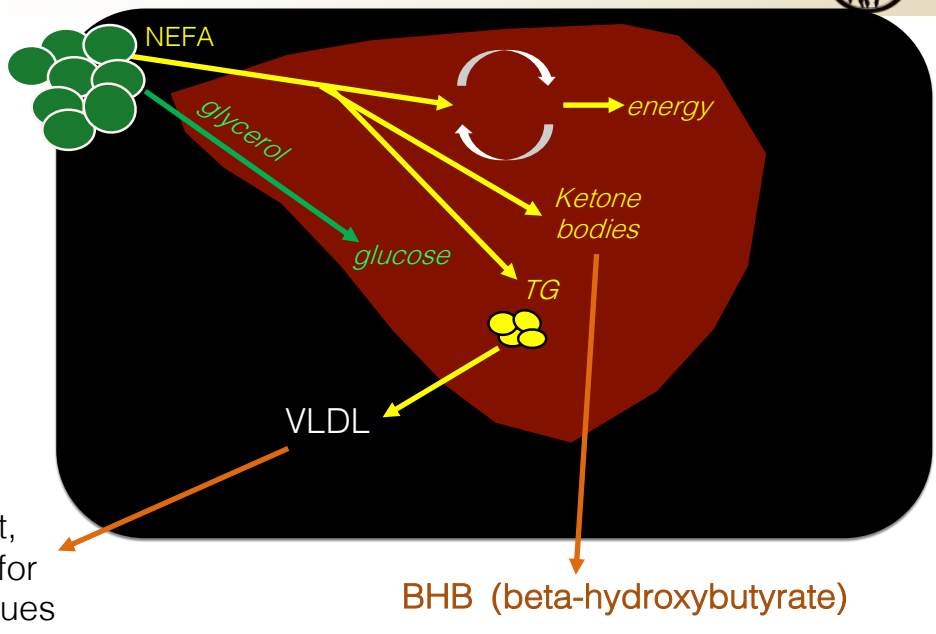
Mobilization of Fat Stores



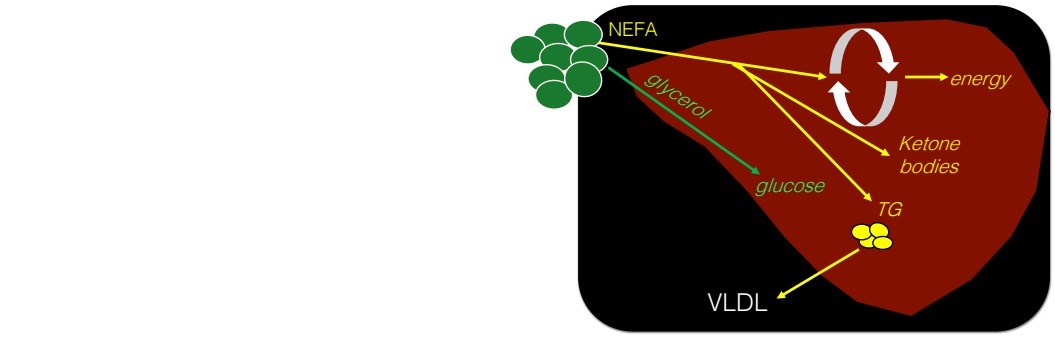
Hepatic Nutrient Partitioning

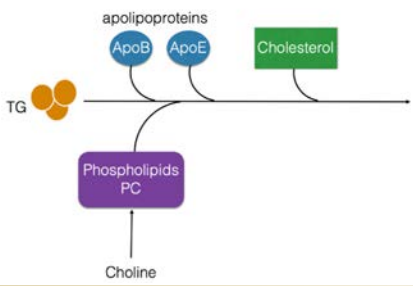


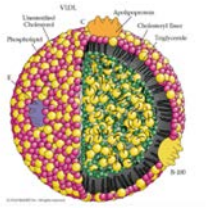
Hepatic Nutrient Partitioning



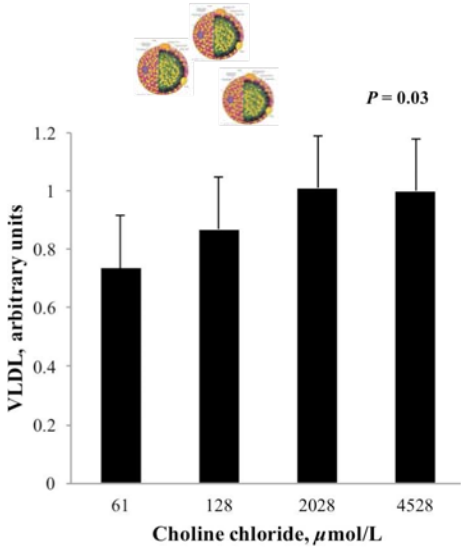
Hepatic Nutrient Partitioning

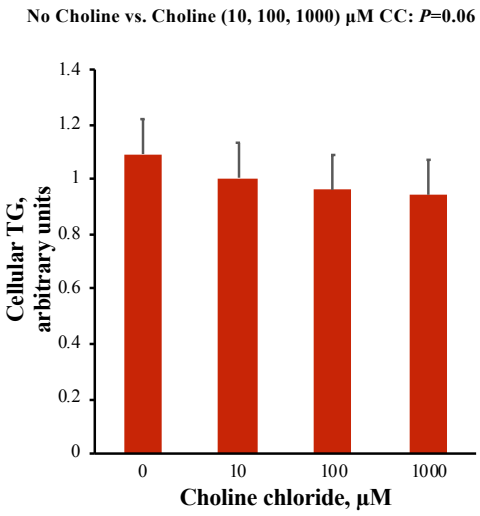


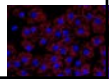




Choline Supplementation Increases VLDL export

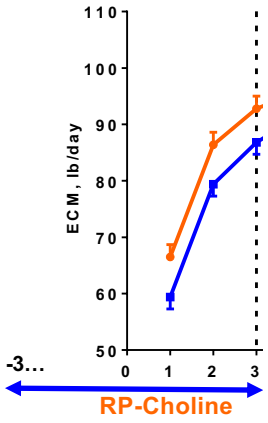






Chandler and White, 2017; Chandler et al., 2019 ADSA abstract

Positive Benefits of RP Choline on Milk Production



Zenobi et al., 2018, JDS 101:1088-1110; 93 Holstein cows

Choline as a Nutritional Intervention

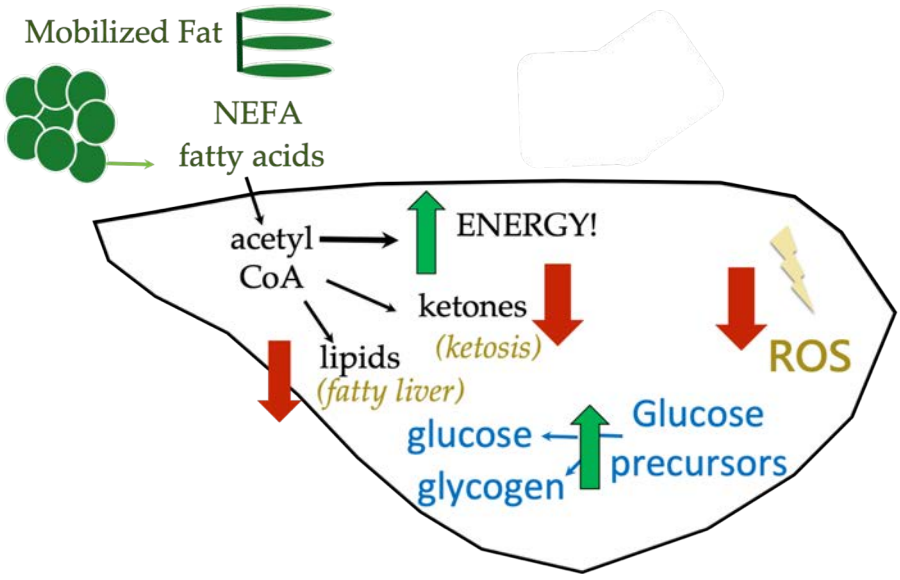
Choline meta analysis of
21 transition cow studies;
66 treatment means; 1,313 cows

- Average supplementation was 12.9 g/d choline ion pre and postpartum
  - Milk yield: 1.6 kg/day
  - Energy-corrected milk: Increased 1.7 kg/day
  - Milk fat yield: Increased 0.07 kg/day
  - Milk protein yield: Increased 0.05 kg/day
  - DMI: Increased pre- and postpartum 0.2 and 0.5 kg/d
- No interactions between prepartum choline and Met, % MP or postpartum average choline (12.9 g/d choline ion) and Met, % MP

Arshad et al., 2020 JDS

What is the mechanism by which choline supports milk production?

Choline Shifts Pathways in Liver Cells



Chandler and White, 2017, 2019; Chandler et al, unpublished

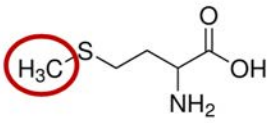
Consistent effects on Hepatocytes

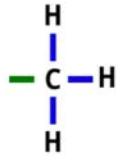
Pathway	Choline Chloride
Lipid Export	↑
VLDL	↓ ✓
TG	
Oxidation	
Complete oxidation (TCA cycle)	↑
BHB production (incomplete oxidation)	↓ ✓
ROS secretion	↓
Glucose Metabolism	↑ ✓
glycogen	
Inflammatory Response	↔
Glutathione production	
Methionine Regeneration (aka methyl donation)	↑ ✓

Chandler and White, 2017, 2019; Chandler et al., 2017 abstract; Zhou et al., 2016; Zhang and White, 2017, 2019; Arshad et al., 2020

Methyl Group Metabolism

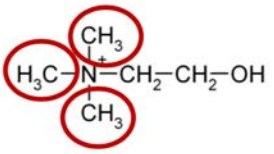
- Methyl groups come from methyl donors
  - methionine (1)



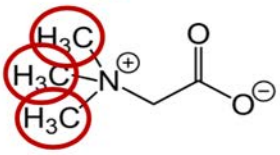


Methyl group

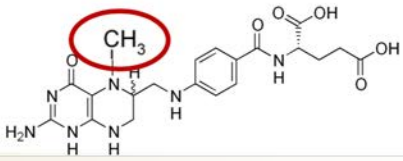
  - choline (3)



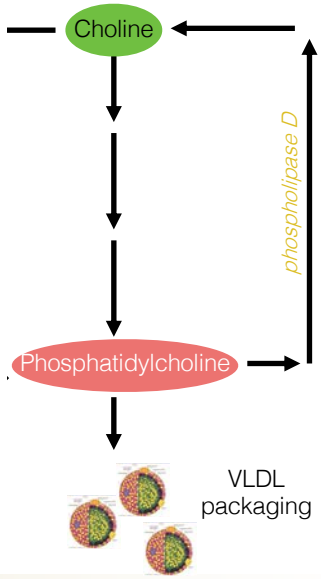
  - betaine (3)



  - folate (5-methyltetrahydrofolate; 1)



Methyl Group Metabolism



Chandler and White, 2017

Consistent effects on Hepatocytes

Pathway	Choline Chloride	Methionine
Lipid Export		
VLDL	↑	↔
TG	↓ ✓	↔
Oxidation		
Complete oxidation (TCA cycle)	↑	↔
BHB production (incomplete oxidation)	↓ ✓	↔
ROS secretion	↓	↔
Glucose Metabolism		
glycogen	↑ ✓	↔
Inflammatory Response		
Glutathione production	↔	↑ ✓
Methionine Regeneration (aka methyl donation)	↑ ✓	Supplied!

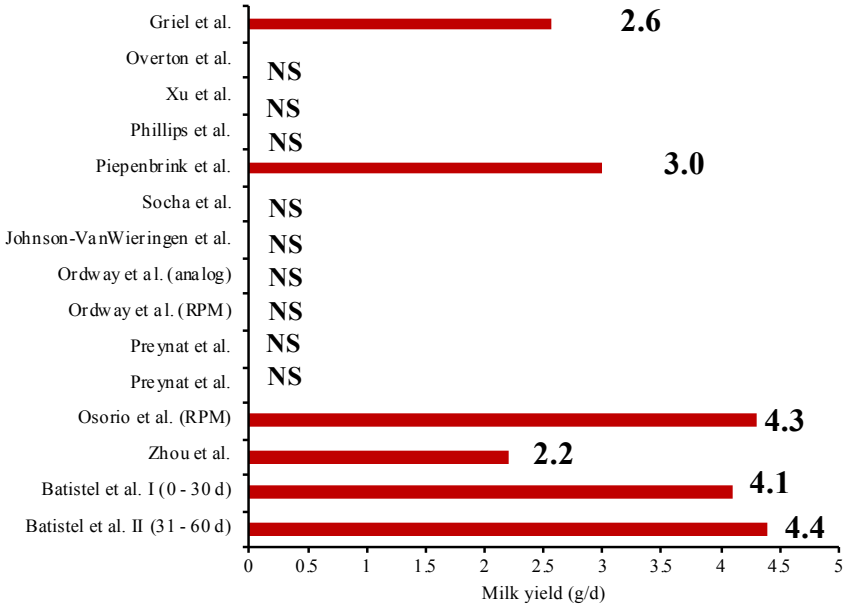
Chandler and White, 2017; Chandler et al., 2016, 2017 abstracts; Zhang and White, 2017, 2019; Zhou et al., 2016; Arshad et al., 2020

Pre- and postpartum Met (RPM and analogs)

Author	Year	Parity	Pre (d)	Post (d)	Extra mMet (g)	n/trt
Griel et al.	1968	-	21	56	-	14
Overton et al.	1996	≥ 2	7 to 10	126	20	12
Xu et al.	1998	≥ 2	21	168-301	8 - 13	14
Phillips et al.	2003	≥ 2	21	120	8	10 - 11
Piepenbrink et al.	2004	≥ 2	21	84	13 - 17	16
Socha et al.	2005	≥ 2	21	42	8	21
Johnson-VanWieringen et al.	2007	1, 2	21	119	7	25
Ordway et al.	2009	1, 2	21	140	12 - 15	20
Preynat et al.	2009	≥ 2	21	112	9.2	10
Preynat et al.	2009	≥ 2	21	112	9.2	6
Osorio et al.	2013	≥ 2	21	30	11 to 12	12 - 14
Zhou et al.	2016	≥ 2	21	30	18	20 - 21
Batistel et al. I	2017	≥ 2	28	1 - 30	15	30
Batistel et al. II				31 - 60	16	

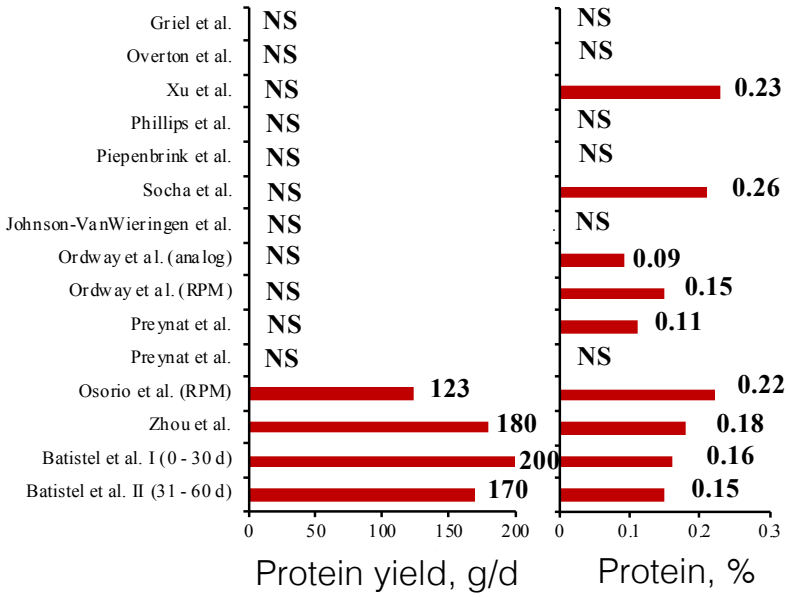
Compiled by Mateus Zucato Toledo

Milk Yield Response



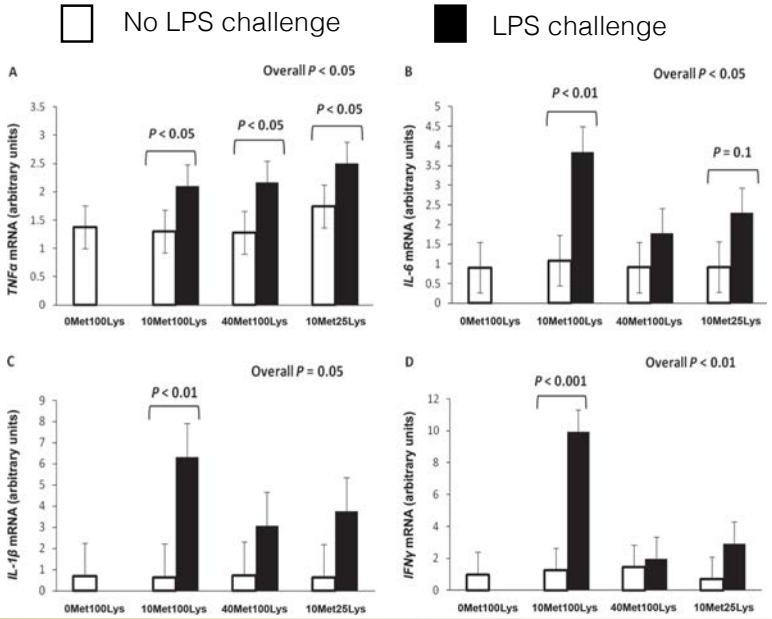
Compiled by Mateus Zucato Toledo

Milk Protein Production Responses



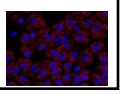
Compiled by Mateus Zucato Toledo

Methionine Ameliorates LPS Challenge

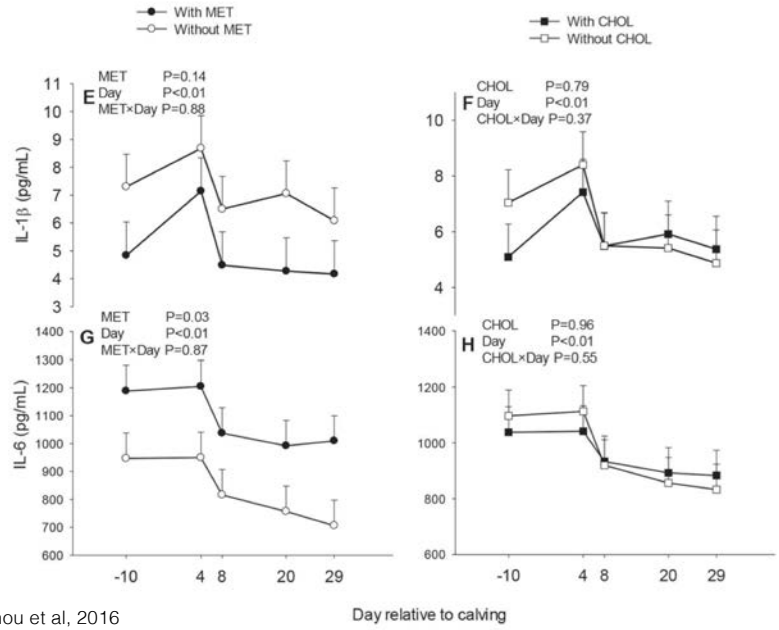


- LPS challenge induces proinflammatory cytokines
- Met mitigates the inflammatory response

Zhang and White, 2017



Methionine Reduces Some Inflammatory Markers During the Transition to Lactation Period



- Calving induces inflammatory response
- Met partially mitigates the inflammatory response

Zhou et al, 2016

Inflammation and Oxidative Stress

- Related but may be more complex than a direct relationship
- Methionine mitigates inflammatory markers and increases glutathione
- Choline decreases ROS without change in glutathione
- We are still learning what these balances mean during the transition to lactation period. . . .

Piecing It All Together

- Supplementation of RP choline results in increased milk yield, ECM, milk protein and fat yield, and increased DMI
  - increased glucose production, complete oxidation, increased VLDL export, and methyl donation
  - decreased lipid accumulation and BHB production
- Supplementation with RP Met or Met analog increases milk yield and milk protein %
  - essential for protein production
  - increased glutathione and ameliorates inflammatory response during LPS challenge and during the transition to lactation period

Take Home Messages

- Both choline and methionine are essential nutrients
- Biological priority for methyl donors (choline and methionine) is apparently different within hepatocytes
- No evidence for choline x Met interaction at average dose in cows or across ranges in cell culture suggests biological priorities in vivo

Acknowledgments

Current White Lab Group


Sophia Erb, Research Specialist


Rafael Oliveira


Ryan Pralle


Henry Holdorf


Malia Martin

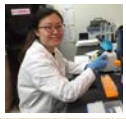
Recent Contributors


Tawny Chandler


Claira Seely


Kristina Weld


Frankie Rathbun


Qian Zhang


Valentina Caprarulo

Collaborators:

Charlie Staples
Marcos Zenobi
Ric Grummer

Research Farm Staff

Funding:

USDA AFRI Foundation 2016-67015-24573
USDA CARE 2015-67028-23572
USDA NSF EAGER 2017-67007-25947
USDA HATCH
UW Foundation
Adisseo, Agsource, Balchem, BASF, and Fermented Nutrition
Student support from Purina and VitaPlus

Questions?